

# EXHIBIT A



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## Prescription opioid mortality trends in New York City, 1990–2006: Examining the emergence of an epidemic★

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### Abstract

**Background**—The drug overdose mortality rate tripled between 1990 and 2006; prescription opioids have driven this epidemic. We examined the period 1990–2006 to inform our understanding of how the current prescription opioid overdose epidemic emerged in urban areas.

**Methods**—We used data from the Office of the Chief Medical Examiner to examine changes in demographic and spatial patterns in overdose fatalities induced by prescription opioids (i.e., analgesics and methadone) in New York City (NYC) in 1990–2006, and what factors were associated with death from prescription opioids vs. heroin, historically the most prevalent form of opioid overdose in urban areas.

**Results**—Analgesic-induced overdose fatalities were the only types of overdose fatalities to increase in 1990–2006 in NYC; the fatality rate increased sevenfold from 0.39 in 1990 to 2.7 per 100,000 persons in 2006. Whites and Latinos were the only racial/ethnic groups to exhibit an increase in overdose-related mortality. Relative to heroin overdose decedents, analgesic and methadone overdose decedents were more likely to be female and to concurrently use psychotherapeutic drugs, but less likely to concurrently use alcohol or cocaine. Analgesic

★Supplementary material can be found by accessing the online version of this paper. Please see Appendix A for more information.

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#### Contributors

M. Cerdá, K. Keyes and S. Galea designed the study and wrote the protocol. M. Cerdá, M. Tracy and Y. Ransome undertook the statistical analyses, and M. Cerdá wrote the first draft of the manuscript. K. Koenen, K. Tardiff and D. Vlahov provided critical input to the revision of manuscript drafts. All authors contributed to and have approved the final manuscript.

#### Conflict of interest

No conflict declared.

Appendix A. Supplementary data

The following are the supplementary data to this article:

overdose decedents were less likely to be Black or Hispanic, while methadone overdose decedents were more likely to be Black or Hispanic in contrast to heroin overdose decedents.

**Conclusions**—The distinct epidemiologic profiles exhibited by analgesic and methadone overdose fatalities highlight the need to define drug-specific public health prevention efforts.

### Keywords

Mortality; Opioid analgesics; Methadone; Overdose; Prescription drugs; Epidemiology; Urban health

## 1. Introduction

Overdose death linked to prescription opioids is a growing public health crisis. The current epidemic accelerated during a fifteen-year interval between 1990 and 2006. In particular, the mortality rate from drug overdose tripled between 1990 and 2006 (CDC, 2010): by 2006, the number of overdose deaths in the United States exceeded the number of suicides; by 2009, they also exceeded the number of motor vehicle deaths. Prescription opioid analgesics, painkillers derived from opium or synthesized to possess narcotic properties similar to opioids, including oxycodone, hydrocodone and codeine, have driven this overdose epidemic (CDC, 2011; Warner et al., 2009). Prescription opioids may have been obtained legally through a prescription, or diverted through illegal distribution networks.

Although much has been written about the epidemic of prescription drug use in rural areas (Green et al., 2011; Hall et al., 2008; Paulozzi et al., 2009; Piercenfield et al., 2010; Shah et al., 2008; Wunsch et al., 2009), the epidemic increase in prescription opioid overdose that occurred between 1990 and 2006 is also reflected in urban areas. For example, from 1997 to 2002, the number of overdose deaths involving prescription opioids increased 97% in metropolitan areas during a time when overdose from all drugs increased only 27% (Paulozzi, 2006). By 2002, prescription opioids were involved in more deaths than heroin or cocaine, the two drugs responsible for most drug abuse in the 1990s (Paulozzi, 2006).

Little information exists on the demographic or spatial patterns of fatal prescription opioid overdose in urban areas in the period leading up to the emergence of the epidemic. Urban studies have focused on the patterns of prescription opioid misuse at one point in time among specific subgroups such as street drug users or marijuana smoking young women (Bardhi et al., 2007; Davis and Johnson, 2008; Lankenau et al., 2012a, 2012b), but to our knowledge, no study has yet examined the longitudinal trends and geographic variation of prescription opioid overdose in a major city in this period.

Therefore, examining the period leading up to the current prescription opioid overdose epidemic in urban areas can lead to important insights. Examining such a period can help us identify new urban patterns of prescription opioid overdose before they become ubiquitous, and can inform our understanding of how future epidemics may emerge.

Studies conducted in primarily rural states, such as the Appalachian, Great Plains and Southwest regions (Green et al., 2011; Hall et al., 2008; Paulozzi et al., 2009; Piercenfield et al., 2010; Shah et al., 2008; Wunsch et al., 2009) can inform our urban research. The highest

increases in fatalities in the period of 1990–2006 occurred among males, persons 35–54 years old, and non-Hispanic Whites (Green et al., 2011; Hall et al., 2008; Paulozzi et al., 2009; Piercenfield et al., 2010; Shah et al., 2008; Warner et al., 2009). Geographic variation has also been noted, with the largest increases found in rural areas and in areas with high retail drug availability (Brownstein et al., 2010; Havens et al., 2007a, 2007b). These secular changes have led to the concentration of prescription opioid overdose deaths in the current time among non-Hispanic White and American Indian/Alaska Native males in rural, low-income areas (Paulozzi et al., 2011). A comprehensive examination of the demographic and geographic variation in prescription opioid overdose fatalities within a city can be critical to help us identify the individual- and contextual-level factors that may be associated with the emergence of this problem in urban areas. Further, an understanding of where prescription opioid overdoses became concentrated in this period can aid in the deployment of surveillance and control efforts.

A critical issue to consider when understanding the emergence of a prescription opioid overdose epidemic in urban areas, is how the profile of prescription opioid overdose differs from that of other types of drug overdose. Prior studies have shown, for example, that prescription opioid overdose decedents are more likely to be older, female, White, and to have concurrently used psychotherapeutic drugs than heroin overdose decedents (Green et al., 2011; Shah et al., 2008). Given the historical focus of urban drug overdose research and prevention efforts on non-prescription drugs, identifying distinctions can facilitate the adaptation of current urban drug prevention strategies.

This study aimed to analyze the epidemiology of prescription opioid-related overdose deaths in New York City (NYC) in the period leading to the emergence of the epidemic (1990–2006) by examining longitudinal trends and geographic differences within this city. In particular, we examined: (1) changes in the epidemiologic patterns of prescription opioid overdose death in NYC in 1990–2006; (2) changes in patterns of spatial variation in prescription opioid overdose deaths across NYC neighborhoods in this time period; and (3) whether the profile of prescription opioid overdose decedents in NYC differed from the profile of heroin overdose decedents, the historically most prevalent form of opioid overdose in urban areas (Bryant et al., 2004; Frank, 2000). Prescription opioid overdose fatalities were examined as two types: analgesic opioid and methadone-induced overdose. Methadone has been prevalent in NYC for decades, and it presents a potentially distinct etiology from analgesic overdose (New York City Department of Health and Mental Hygiene, 2011).

## 2. Methods

### 2.1. Study population

Cases of fatal unintentional poisoning deaths (ICD-10 codes X40–X44, T40.0–T40.2) occurring in adults aged 15–64 years in NYC between 1990 and 2006 were identified through manual review of medical files at the Office of the Chief Medical Examiner of NYC (OCME) from 1990 to 2006. The OCME is responsible for investigating all deaths of people believed to have died from unnatural causes. Thus, all overdose deaths in NYC are reviewed by the OCME and would have been included in the charts used for data extraction.

## 2.2. Data collection

Decedent's medical history, the circumstances and environment of the death, autopsy findings, and laboratory data were used to attribute the cause of death to each case reviewed. Hence, classification of cause of death differs from simple presence or absence of a drug in a toxicological screen. Decedents with positive screens for a prescription opioid will not necessarily be classified as a prescription opioid-induced death, they may, instead, be classified as other types of accidental, non-overdose deaths or intentional deaths.

Attributions of drugs as a cause of death by the OCME are not mutually exclusive: an overdose death may be attributed to more than one drug. Medical Examiner systems have shown high sensitivity, specificity and positive predictive value to identify external causes of death (Comstock et al., 2005; Landen et al., 2003; Sternfeld et al., 2010). Data regarding cause of death, circumstances of death, and toxicology were collected from the OCME files by trained abstractors using a standardized protocol and data collection forms. Further details on overdose data collection are provided in Galea et al. (2003).

Cases of unintentional overdose death in which a prescription opioid was cited as a cause of death, alone or in combination with other drugs, were classified as prescription opioid overdose deaths. Prescription opioids were classified as two types: (1) analgesic opioids (hereafter referred to as "analgesics"), including codeine, fentanyl, hydrocodone, hydromorphone, meperidine, morphine, oxycodone, and propoxyphene (the proportion of analgesic drug overdose deaths due to each type of analgesic drug is presented as online Supplementary Material<sup>1</sup>) and (2) methadone. Unintentional deaths with an undetermined cause, as well as overdose deaths with an undetermined drug that caused the overdose, were not included in the study. Deaths caused by intentional injury are not considered accidents by the OCME; hence, overdose deaths due to suicide were not considered in this study. Of all opioid-induced deaths, only 0.5% were listed as undetermined or suicide.

## 2.3. Covariates

To characterize the decedents from prescription opioid overdose, we abstracted the following characteristics from the OCME file: decedent sex, age, place of injury, and NYC borough of death. We also examined the proportion of prescription opioid overdose deaths in which heroin overdose was also a contributing cause, and the proportion of prescription opioid overdose deaths with positive toxicology reports for non-opioid substances, including alcohol, cannabinoids, cocaine, benzodiazepines, and antidepressants. The latter substances were detected but not considered primary causes of death in the cases of prescription opioid overdose deaths. A list of the benzodiazepine and antidepressant drugs detected is presented as online Supplementary Material.<sup>2</sup>

## 2.4. Statistical analyses

To fulfill our first objective of examining changes in epidemiologic patterns of analgesic overdose death, we followed three steps. We first compared the evolution of overdoses caused by prescription opioids to overdoses caused by other leading types of drugs. We

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<sup>1</sup>Supplementary material can be found by accessing the online version of this paper. Please see Appendix A for more information.

<sup>2</sup>Supplementary material can be found by accessing the online version of this paper. Please see Appendix B for more information.

calculated the overdose death rate per 100,000 person-years by leading type of drugs (single and polydrug-induced overdose by cocaine, heroin, alcohol, methadone and analgesics) for each year from 1990 to 2006. To determine the rate denominators, we obtained total, age-, sex-, and race/ethnic-specific population counts for New York City for 1990 and 2000 from the Census Summary File 3 and for 2005–2006 from the American Community Survey (ACS) 2005–2009 (United States Census Bureau, 2012a, 2012b, 2012c). Population counts for the intervening years were computed using linear interpolation. We standardized cause-specific overdose mortality rates for New York City by age, sex, and race to the 2000 census for New York City to enable comparability between years in the analysis (Galea et al., 2003). A non-parametric test of trend across ordered groups was used to assess the significance of changes in the rates of drug-specific-induced deaths over time (Cuzick, 1985).

Second, we examined the evolution of prescription opioid overdose by race/ethnicity and sex. We calculated prescription opioid overdose death rates between 1990 and 2006 stratified by race and sex. We focused on the three largest racial/ethnic groups: White, Black and Latino. Thus, we calculated the age-standardized rate of overdose deaths caused by analgesics and methadone for White males, White females, Black males, Black females, Latino males, and Latino females.

Third, we examined whether the patterns of co-occurring non-opioid drugs detected varied over time. In particular, we used a non-parametric test of trend to test whether the proportion of analgesic and methadone overdose fatalities with positive toxicology reports for non-opioid drugs (specifically, alcohol, cannabinoids, cocaine, benzodiazepines, and antidepressants) differed over time.

To fulfill our second objective of investigating changes in patterns of spatial variation in analgesic overdose deaths, we presented the spatial distribution of prescription opioid overdose death rates in 1990–1995, 1996–2000, and 2001–2006 across NYC neighborhoods. All OCME analgesic opioid overdose cases in 1990–2006 were geocoded to the neighborhood level by address of injury using ArcGIS software, version 9.0 (ESRI, 2011). Only cases with a valid address of injury (i.e., 88%) were included in the analysis; these cases did not differ in demographic characteristics from cases without a valid address of injury.

Neighborhoods consist of adjoining zip codes, designated to approximate New York City Community Planning Districts. The assignment of zip code areas to neighborhoods, the decisions about which community planning districts were most appropriate to combine, and the delineation of neighborhoods were made by the Department of City Planning in consultation with local residents. The 59 neighborhood boundaries have remained unchanged between the 1990 and 2000 census (New York City Department of City Planning, 2012).

Age-adjusted rates were calculated for each year and then averaged for each five-year grouping. Small neighborhood-and year-specific cell sizes by sex, age and race/ethnicity impeded us from constructing age-, sex- and race/ethnicity-adjusted neighborhood rates.



Rates were smoothed using an Empirical Bayes technique to improve stability in areas with large populations and very few cases (Pfeiffer, 2008). Data were then mapped to the 59 community districts using ArcMap 10.0 (ESRI, 2011). To characterize the spatio-temporal variation in prescription opioid overdose mortality, we used bivariate Moran's *I* statistics and estimated the correlation between neighborhood distribution of overdose deaths in 1990–1995 and 1996–2000, as well as between 1996–2000 and 2001–2006. Spatial statistics were estimated using GeoDa 1.20.

Our third objective was to compare the demographic and behavioral characteristics (e.g., age, sex, race/ethnicity, concurrent drug toxicology) of prescription opioid overdose vs. heroin overdose deaths. To this end, logistic regression was used to examine the bivariable and multivariable relations between each of the decedent characteristics of interest and the likelihood of overdose deaths caused by: (1) analgesics alone compared to heroin alone and (2) methadone alone compared to heroin alone. All models controlled for year of death. Given the low frequency of overdose fatalities in places other than residence, the places of residence were grouped into inside (representing “inside residence”), other inside (i.e., workplace, jail/prison, hospital/doctor's office/nursing home, hotel, bar/restaurant, building), and outside (i.e., public transportation or car, street/lots/school yard, parks or water) for this analysis. Models were estimated in SAS 9.2 (SAS Institute Inc., 2002–2008).

### 3. Results

Analgesic and methadone overdose deaths are described in Table 1 and indicate that deaths were most common among middle-aged adults and males. While analgesic overdose was most frequent among Whites, methadone overdose was evenly distributed across Whites, Blacks and Hispanics. Heroin was a contributing cause in 44.6% of analgesic- and 39.9% of methadone-induced overdose fatalities. The majority of deaths occurred in a residence (82.7% of analgesic- and 79.9% of methadone-induced deaths), and deaths were evenly distributed across the largest NYC boroughs (Manhattan, Bronx, Brooklyn, and Queens). The most frequently detected non-opioid drugs were cocaine (45.7% of analgesic- and 53.2% of methadone-induced deaths), followed by antidepressants (37.4% of analgesic- and 37.3% of methadone-induced deaths).

#### 3.1. Changes in epidemiologic patterns of prescription opioid overdose death

Prescription opioid deaths evolved in a distinct manner from other drugs in 1990–2006, the years leading to the emergence of the analgesic opioid overdose epidemic (Fig. 1). Cocaine-, heroin- and alcohol-induced deaths peaked in 1993–1995 with rates of 15.5/100,000, 14.1/100,000 and 6.9/100,000, respectively. In contrast, methadone-induced deaths peaked in 1991 (3.2/100,000) and in 2006 (4.4/100,000), while analgesic-induced deaths increased steadily starting in 1999 and reached their highest rates (2.7/100,000) in 2006. Analgesic overdose fatalities were the only types of overdose to exhibit significantly increasing trends from 1990 to 2006 (*Z test of trend statistic* = 3.13, *P* < 0.01); the analgesic overdose rate was almost seven times higher in 2006 than in 1990. The proportion of all overdose deaths caused by analgesics increased from 3.9% to 15.6% while the proportion of overdose deaths caused by methadone overdose fatalities increased from 15.9% to 25.1% in 1990–2006.

The increase in analgesic overdose was driven by increased rates among White and Latinos, particularly males (Fig. 2a). In 1990, analgesic overdose rates were 0.62 for White, 0.56 for Latino and 0.41/100,000 for Black males; by 2006, the rates were 6.00 for White, 3.58 for Latino and 2.22/100,000 for Black males. Only White and Latino males exhibited a significant increase in analgesic overdose from 1990 to 2006 (*Z test of trend statistic* = 3.54;  $P < 0.01$  and *Z test of trend statistic* = 2.39;  $P < 0.05$ , respectively). Among females, Whites and Latinas also exhibited a significant increase in analgesic overdose fatalities from 1990 to 2006 (*Z test of trend statistic* = 2.81;  $P < 0.01$  and *Z test of trend statistic* = 2.03;  $P < 0.05$ , respectively). In 1990, analgesic overdose rates were 0.31 for White, 0.27 for Latino and 0.11 for Black females; by 2006, the rates were 1.71 for White, 1.66 for Latino and 0.91 for Black females.

The demographic profile of methadone overdose deaths also shifted from 1990 to 2006 (Fig. 2b). In 1990, methadone rates were 0.88 for White, 3.14 for Latino and 5.05/100,000 for Black males; by 2006, the rates were 7.82 for White, 6.77 for Latino and 3.68 for Black males. Only White males exhibited a significant increase in methadone overdose deaths in this period (*Z test of trend statistic* = 2.83;  $P < 0.01$ ), while Black males exhibited a significant decrease in methadone overdose deaths in the same period (*Z test of trend statistic* = 2.22;  $P < 0.05$ ). Among females, Whites also exhibited a significant increase in methadone overdose fatalities from 1990 to 2006 (*Z test of trend statistic* = 3.00;  $P < 0.01$ ). In 1990, methadone overdose rates were 0.47 for White, 1.48 for Latina and 1.25 for Black females; by 2006, the rates were 1.96 for White, 3.16 for Latina and 2.84 for Black females.

The temporal patterns of co-occurring drugs detected differed for analgesic and methadone overdose fatalities. Fig. 3a and b presents the proportion of analgesic and methadone overdose deaths, respectively, with positive toxicology for different types of non-opioid substances. The types of drugs detected in cases of analgesic overdose deaths did not vary over time, with the exception of cannabinoids; the proportion of analgesic overdose cases with a positive toxicology report for cannabinoids increased over time ( $Z = 2.22$ ;  $P = 0.03$ ). In contrast, the types of drugs detected in cases of methadone overdose deaths varied over time: while the proportion of cases with positive toxicology for alcohol ( $Z = -2.37$ ;  $P = 0.02$ ) or cocaine ( $Z = -2.89$ ;  $P = 0.004$ ) decreased overtime, the proportion of cases with positive toxicology for cannabinoids ( $Z = 2.06$ ;  $P = 0.04$ ), or benzodiazepines ( $Z = 2.5$ ;  $P = 0.01$ ) increased overtime.

### 3.2. Spatial patterns of prescription opioid overdose mortality

The rates of analgesic and methadone overdose mortality followed distinct spatial patterns over time. As shown by the distribution of analgesic overdose mortality rates in Fig. 4, clustering of analgesic overdose deaths shifted in space over time. There was no correlation between the neighborhoods with higher rates of analgesic overdose deaths in 1990–1995 and 1996–2000 (bivariate Moran's  $I = -0.02$ ;  $P = 0.48$ ), or the neighborhoods with higher rates in 1996–2000 and 2001–2006 ( $I = -0.01$ ;  $P = 0.55$ ). In contrast, clusters of neighborhoods with high rates of methadone overdose surrounded by other neighborhoods with high rates remained stable over time (Fig. 4). There was a high and significant correlation between neighborhoods with higher methadone overdose death rates in 1990–1995 and 1996–2000 ( $I$



= 0.45;  $P = 0.001$ ), and between the spatial distribution of methadone overdose death rates in 1996–2000 and 2001–2006 ( $I = 0.43$ ;  $P = 0.001$ ).

### 3.3. Differences in epidemiologic patterns of prescription opioid and heroin overdose deaths

Prescription opioid-only overdose deaths presented different demographic and behavioral characteristics from heroin overdose deaths (Table 2). Relative to heroin overdose decedents, decedents from analgesic-only or methadone overdose-only were more likely to be female. Overdose fatalities induced by analgesics or methadone were less likely to occur outside of a residence than heroin overdose fatalities, and they were less likely to involve alcohol or cocaine. They were more likely to involve the use of benzodiazepines and antidepressants. Relative to heroin overdose decedents, analgesic overdoses were less likely to be experienced by Blacks or Hispanics, and they were more likely to occur in Queens or Staten Island. In contrast, decedents from methadone overdose were more likely to be Black or Hispanic and to have overdosed in Staten Island than heroin overdose decedents.

## 4. Discussion

The period from 1990 to 2006 was a time of significant growth in analgesic overdose fatalities in NYC. While methadone overdose remained stable, the rate of analgesic overdose deaths in NYC in 2006, at 2.7 per 100,000 persons, was almost seven times higher than the rate in 1990; indeed, analgesic overdose was the only type of overdose fatality to escalate in this period. Increased rates of analgesic overdose fatalities can be driven by increased rates of analgesic use and misuse, as well as by changes in the rate of mortality among users who overdosed. The parallel sharp increase in rates of use (Blanco et al, 2007; Zacny et al., 2003) and abuse/dependence (Blanco et al., 2007) in the study period suggests that a major contributor to the escalation in analgesic overdose mortality were the growing rates of analgesic use and abuse that followed the tenfold increase in the medical use of opioids since 1990 (Okie, 2010). In 1997–2007, per capita retail purchases of hydrocodone and oxycodone increased 4-fold and 9-fold, respectively (ARCOS: Automation of Reports and Consolidated Orders System, 2012); sales, substance abuse treatment admissions and overdose death rates have increased in parallel (CDC, 2011).

Due to the focused rise in analgesic opioid overdose fatalities among Whites, the gap across racial/ethnic groups increased over time, so that by 2006, the analgesic overdose fatality rate among White males was almost two times higher than the rate among Latinos and almost three times higher than the rate among Blacks. These inequalities are consistent with patterns found elsewhere: at a national level, the analgesic overdose rate among Whites was three times higher than rates in Blacks and Latinos (CDC, 2011); state-level studies reported similar findings (Piercenfield et al., 2010; Shah et al., 2008). The differences may reflect different patterns of drug use in the different racial/ethnic groups throughout the sixteen years of study. Prior studies have found that Blacks are more likely to overdose on cocaine, while Whites and Latinos are more likely to overdose on opioids and alcohol (Coffin et al., 2003; Galea et al., 2003). In the case of analgesics, racial/ethnic differences in access may play an important role, given the same clinical presentation and report of pain level, racial/

ethnic minorities are less likely to receive a prescription for an analgesic (Green et al., 2005; Mayer et al., 2008). Price may also play a role (Greenwald and Hursh, 2006); the lower price of heroin relative to analgesics may create an economic disincentive for racial/ethnic minorities to consume analgesics.

Methadone overdose fatalities also experienced a demographic shift, by 2006, the methadone overdose fatality rate among Whites was two times higher than the rate among Blacks. While methadone overdose rates among Whites increased almost nine-fold in 1990–2006, overdose rates among Blacks decreased by 27% in the same period. Concurrently, the pattern of co-occurring drugs detected with methadone shifted from cocaine to cannabinoids and benzodiazepines. These changes may reflect the shift in the nature of methadone use, from a focused use as a treatment for heroin addiction, primarily among racial/ethnic minorities with a history of substance abuse, to increasing use as a treatment for chronic non-cancer pain, in conjunction with analgesics and other types of prescription drugs (Paulozzi et al., 2009; Paulozzi, 2012).

Analgesic and methadone overdose fatalities exhibited strikingly different spatial patterns over time. While clusters of analgesic overdose fatalities shifted spatially from 1990 to 2006, methadone overdose fatalities were concentrated in the same neighborhoods from 1990 to 2006. The distinct spatio-temporal patterns exhibited by analgesics vs. methadone suggest that each type of prescription opioid may also be associated with distinct contextual factors. To provide local context, it is worth noting that the neighborhoods with high rates of analgesic overdose fatalities were characterized by high income inequality but lower rates of poverty in the year 2000 (United States Census Bureau, 2000). In contrast, methadone overdose fatalities were consistently concentrated in neighborhoods with high income inequality, high rates of poverty and lower median income (United States Census Bureau, 2000). Future studies need to investigate the role that contextual factors play in the proliferation of analgesic vs. methadone overdose fatalities over time.

Despite high rates of co-occurrence with heroin, prescription opioid overdose presents a different etiologic profile from heroin overdose. In our study, methadone and analgesic opioid decedents were less likely to present traces of alcohol or cocaine than heroin overdose decedents, but they were more likely to show traces of psychotherapeutic drugs such as benzodiazepines and antidepressants. They were also more likely to be female than heroin overdose decedents, and to overdose at home. Studies in other states also found that prescription opioid overdose decedents were more likely to be female and have co-occurring use of psychotherapeutic drugs (Green et al, 2011; Shah et al., 2008). These findings indicate that the prescription opioid consumer may be quite distinct from the heroin consumer, showing a lower involvement in street-based forms of drug trafficking, access and consumption, and less comorbid consumption of drugs such as cocaine. Given the increasing rates of prescription opioid overdose fatalities in urban areas such as NYC, we may need to develop a distinct response to this problem.

This study is subject to several limitations. First, the OCME classified certain deaths as caused by “unspecified opioids” and some of these cases may be methadone or analgesic overdose deaths, leading to an underestimate of the prevalence of prescription opioid

overdose in our study. Second, we had no information on the source of prescription opioids, i.e., whether it had been obtained from a licensed provider or from a third party. Third, data was only available until 2006. Subsequent trends remain to be analyzed once more recent data becomes accessible. However, an examination of the demographic profile of prescription opioid overdose fatalities in a period that experienced dramatic growth in prescription opioid overdose provided critical information on potential factors associated with the proliferation of prescription opioid abuse.

Early recognition of drug abuse patterns is critical to the design of strategies that prevent use and abuse from spreading and stop an epidemic before it emerges. This study provides insights about the emergence of an analgesic opioid epidemic in a large, multiethnic urban area, as well as a potentially developing methadone overdose epidemic among White residents who may use methadone to treat chronic pain. Our findings suggest that in order to prevent the development of a prescription opioid epidemic, steps in the 1990s to increase the availability and use of analgesics, including aggressive marketing of potent formulations such as oxycodone hydrochloride and efforts to encourage clinicians to be more proactive in identifying and treating chronic pain, should have been accompanied by stricter measures to regulate sales of analgesics and to prevent the proliferation of illicit high-volume prescribers (Boudreau et al., 2009; Paulozzi et al., 2006). At the current time, effective reduction of prescription opioid overdose deaths in NYC will require localized interventions, including real-time prescription monitoring programs, that shape availability and access to prescription drugs, focused action by law enforcement to identify networks of illicit distribution of prescription opioids, policies to increase naloxone dispensation to reduce fatalities from overdose, increased use of buprenorphine rather than methadone for harm reduction, and education of physicians and health care providers about prescription drug abuse and overdose (Pew Health Group, 2012).

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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## References

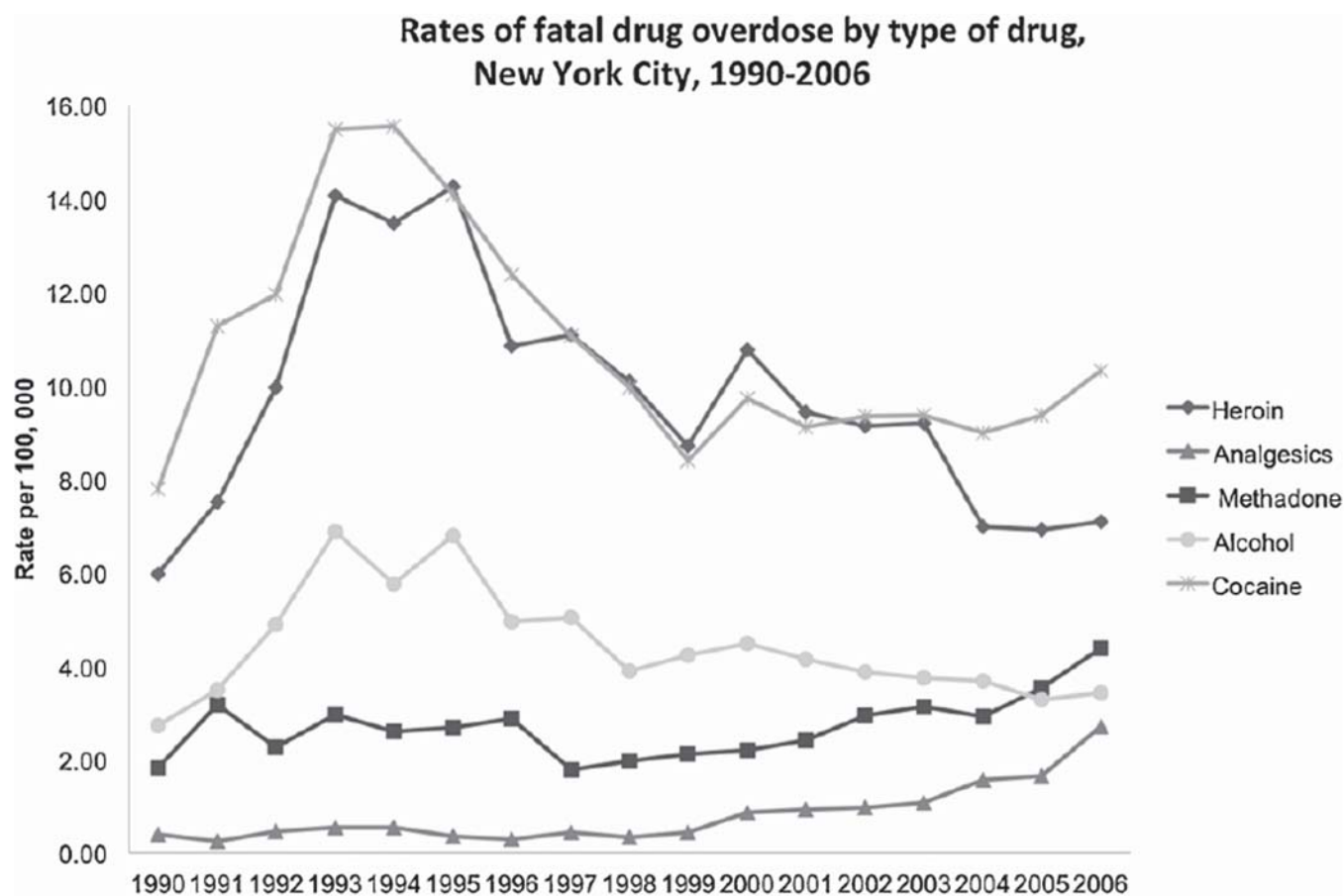
- ARCOS: Automation of Reports and Consolidated Orders System. [accessed 2012] <http://www.deadiversion.usdoj.gov/arcos/index.html>. Archived by WebCite at <http://www.webcitation.org/67UIDqkGN>
- Bardhi F, Sifaneck SJ, Johnson BD, Dunlap E. Pills, thrills and bellyaches: case studies of prescription pill use and misuse among marijuana/blunt smoking middle class young women. *Contemp. Drug Probl.* 2007; 34:53–101. [PubMed: 19081798]

- Blanco C, Alderson D, Ogburn E, Grant BF, Nunes EV, Hatzenbuehler ML, Hasin DS. Changes in the prevalence of non-medical prescription drug use and drug use disorders in the United States: 1991–1992 and 2001–2002. *Drug Alcohol Depend.* 2007; 90:252–260. [PubMed: 17513069]
- Boudreau D, Von Korff M, Rutter CM, Saunders K, Ray GT, Sullivan MD, Campbell CI, Merrill JO, Silverberg MJ, Banta-Green C, Weisner C. Trends in long-term opioid therapy for chronic non-cancer pain. *Pharmacoepidemiol. Drug Saf.* 2009; 18:1166–1175. [PubMed: 19718704]
- Brownstein JS, Green TC, Cassidy TA, Butler SF. Geographic information systems and pharmacoepidemiology: using spatial cluster detection to monitor local patterns of prescription opioid abuse. *Pharmacoepidemiol. Drug Saf.* 2010; 19:627–637. [PubMed: 20535759]
- Bryant WK, Galea S, Tracy M, Piper TM, Tardiff KJ, Vlahov D. Overdose deaths attributed to methadone and heroin in New York City, 1990–1998. *Addiction.* 2004; 99:846–854. [PubMed: 15200580]
- CDC. [accessed 2012] WONDER. 2010. <http://wonder.cdc.gov>. Archived by WebCite at <http://www.webcitation.org/67U13jeg2>
- CDC. Vital signs: overdoses of prescription opioid pain relievers – United States, 1999–2008. *MMWR.* 2011; 60:1487–1492. [PubMed: 22048730]
- Coffin PO, Galea S, Ahern J, Leon AC, Vlahov D, Tardiff K. Opiates, cocaine and alcohol combinations in accidental drug overdose deaths in New York City, 1990–98. *Addiction.* 2003; 98:747–793.
- Comstock RD, Mallonee S, Jordan F. A comparison of two surveillance systems for deaths related to violent injury. *Inj. Prev.* 2005; 11:58–63. [PubMed: 15691992]
- Cuzick J. A Wilcoxon-type test for trend. *Stat. Med.* 1985; 4:87–90. [PubMed: 3992076]
- Davis WR, Johnson BD. Prescription opioid use, misuse, and diversion among street drug users in New York City. *Drug Alcohol Depend.* 2008; 92:267–276. [PubMed: 17913395]
- ESRI. ArcGIS Desktop: Release 10. Redlands, CA: Environmental Systems Research Institute; 2011.
- Frank B. An overview of heroin trends in New York City: past, present and future. *Mt. Sinai J. Med.* 2000; 67:340–346. [PubMed: 11064484]
- Galea S, Ahern J, Tardiff K, Leon AC, Coffin PO, Derr K, Vlahov D. Racial/ethnic disparities in overdose mortality trends in New York City, 1990–1998. *J. Urban Health.* 2003; 80:201–211. [PubMed: 12791796]
- Green CR, Ndao-Brumblay SK, West B, Washington T. Differences in prescription opioid analgesic availability: comparing minority and white pharmacies across Michigan. *J. Pain.* 2005; 6:689–699. [PubMed: 16202962]
- Green TC, Grau LE, Carver HW, Kinzly M, Heimer R. Epidemiologic trends and geographic patterns of fatal opioid intoxications in Connecticut, USA: 1997–2007. *Drug Alcohol Depend.* 2011; 115:221–228. [PubMed: 21131140]
- Greenwald MK, Hursh SR. Behavioral economic analysis of opioid consumption in heroin-dependent individuals: effects of unit price and pre-session drug supply. *Drug Alcohol Depend.* 2006; 85:35–48. [PubMed: 16616994]
- Hall AJ, Logan JE, Toblin RL, Kaplan JA, Kraner JC, Bixler D, Crosby AE, Paulozzi LJ. Patterns of abuse among unintentional pharmaceutical overdose fatalities. *JAMA.* 2008; 300:2613–2620. [PubMed: 19066381]
- Havens JR, Oser CB, Leukefeld CG, Webster JM, Martin SS, O’Connell DJ, Surratt HL, Inciardi JA. Differences in prevalence of prescription opiate misuse among rural and urban probationers. *Am. J. Drug Alcohol Abuse.* 2007a; 33:309–317. [PubMed: 17497554]
- Havens JR, Walker R, Leukefeld CG. Prevalence of opioid analgesic injection among rural nonmedical opioid analgesic users. *Drug Alcohol Depend.* 2007b; 87:98–102. [PubMed: 16959437]
- Landen MG, Castle S, Nolte KB, Gonzales M, Escobedo LG, Chatterjee BF, Johnson K, Sewell CM. Methodological issues in the surveillance of poisoning, illicit drug overdose, and heroin overdose deaths in New Mexico. *Am. J. Epidemiol.* 2003; 157:273–278. [PubMed: 12543628]
- Lankenau SE, Schrager SM, Silva K, Kecojevic A, Bloom JJ, Wong C, Iverson E. Misuse of prescription and illicit drugs among high-risk young adults in Los Angeles and New York. *J. Public Health Res.* 2012a; 1:22–30. [PubMed: 22798990]

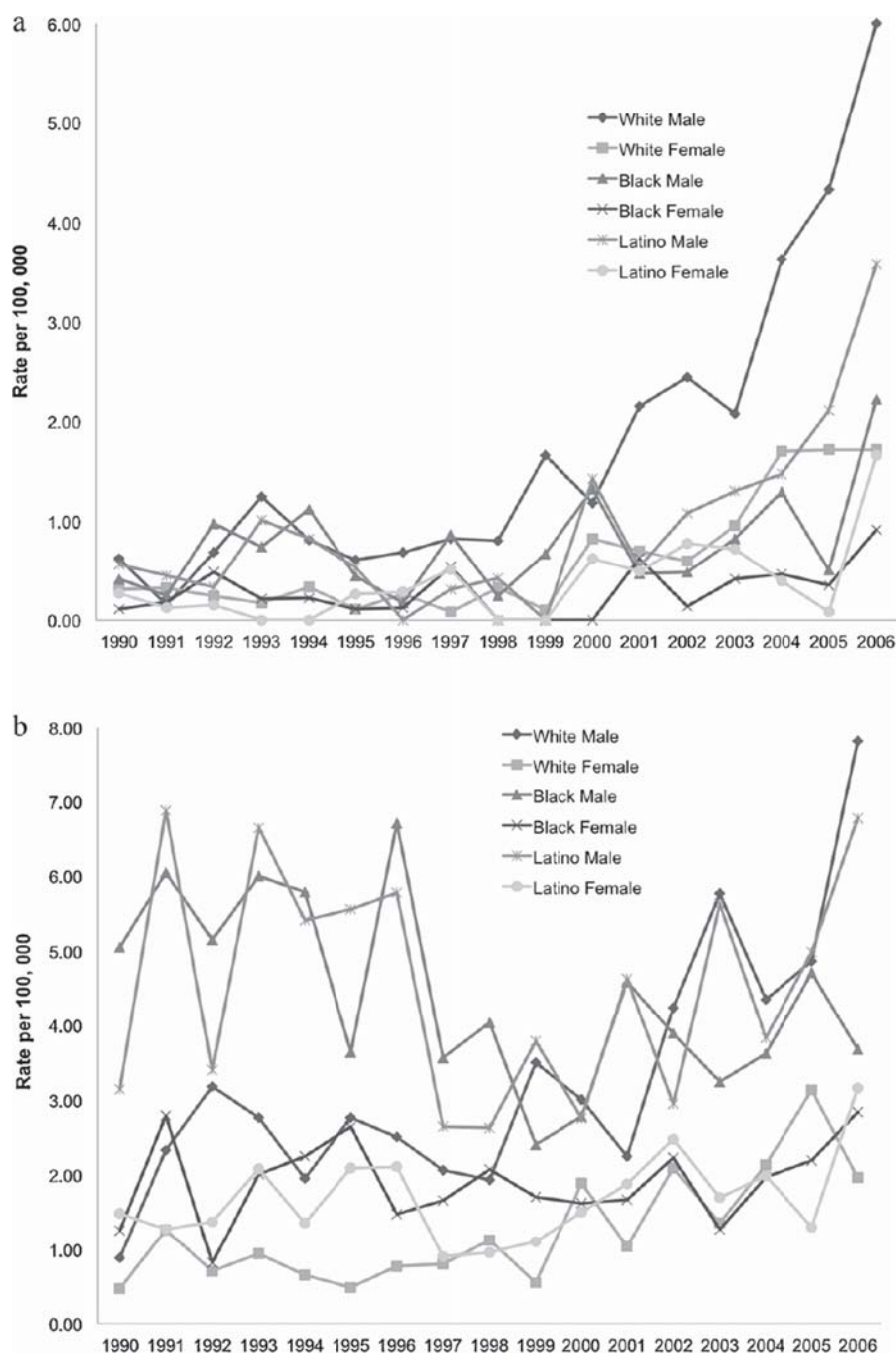
- Lankenau SE, Teti M, Silva K, Bloom JJ, Harocopos A, Treese M. Patterns of prescription drug misuse among young injection drug users. *J. Urban Health*. 2012b; 89:1004–1016. [PubMed: 22684424]
- Mayer JD, Kirlin B, Rehm CD, Loeser JD. Opioid availability in outpatient pharmacies in Washington State. *Clin. J. Pain*. 2008; 24:120–123. [PubMed: 18209517]
- New York City Department of City Planning. [accessed 18.09.12] Bytes of the Big Apple. 2012. <http://www.nyc.gov/html/dcp/html/bytes/applbyte.shtml>
- New York City Department of Health and Mental Hygiene. Opioid analgesics in New York City: misuse, morbidity and mortality update. *Epi Data Brief* 3. 2011
- Okie S. A flood of opioids, a rising tide of deaths. *N. Engl. J. Med*. 2010; 363:1981–1985. [PubMed: 21083382]
- OpenGeoDa for Windows version 1.20. GeoDa Center for Geospatial Analysis and Computation. Tempe, AZ: Arizona State University;
- Paulozzi L. Vital signs: risk for overdose from methadone used for pain relief: United States, 1999–2010. *MMWR*. 2012; 61:493–497. [PubMed: 22763888]
- Paulozzi LJ. Opioid analgesic involvement in drug abuse deaths in American metropolitan areas. *Am. J. Public Health*. 2006; 96:1755–1757. [PubMed: 17008568]
- Paulozzi LJ, Budnitz DS, Xi Y. Increasing deaths from opioid analgesics in the United States. *Pharmacoepidemiol. Drug Saf*. 2006; 15:618–627.
- Paulozzi LJ, Jones C, Mack K, Rudd R. Vital signs: overdoses of prescription opioid pain relievers – United States, 1999–2008. *MMWR*. 2011; 60:1487–1492. [PubMed: 22048730]
- Paulozzi LJ, Logan JE, Hall AJ, McKinstry E, Kaplan JA, Crosby AE. A comparison of drug overdose deaths involving methadone and other opioid analgesics in West Virginia. *Addiction*. 2009; 104(9):1541–1548. [PubMed: 19686524]
- Pew Health Group. [accessed 30.11.12] As Painkiller Overdoses Mount, Researchers Outline Effective Approaches to Curb Epidemic. 2012. <http://www.sciencedaily.com/releases/2012/09/120920140202.htm>
- Pfeiffer, D. *Spatial Analysis in Epidemiology*. Oxford: Oxford University Press; 2008.
- Piercenfield E, Archer P, Kemp P, Mallonee S. Increase in unintentional medication overdose deaths: Oklahoma, 1994–2006. *Am. J. Prev. Med*. 2010; 39:357–363. [PubMed: 20837287]
- SAS Institute Inc. SAS 9.2. Cary, NC: 2002–2008.
- Shah NG, Lathrop SL, Reichard RR, Landen MG. Unintentional drug overdose death trends in New Mexico, USA, 1990–2005: combinations of heroin, cocaine, prescription opioids and alcohol. *Addiction*. 2008; 103:126–136. [PubMed: 18028518]
- Sternfeld I, Perras N, Culross PL. Development of a coroner-based surveillance system for drug-related deaths in Los Angeles County. *J. Urban Health*. 2010; 87:656–669. [PubMed: 20440654]
- United States Census Bureau. Data derived from Population Estimates, 2000 Census of Population and Housing. Washington, DC: 2000. State and Country Quick Facts.
- United States Census Bureau. [accessed January 2012] 1990 Census Summary File 3: New York (Bronx, Kings, New York, Queens, Richmond). 2012a. [http://www2.census.gov/census\\_1990/CD90\\_3A\\_40/](http://www2.census.gov/census_1990/CD90_3A_40/). Archived by WebCite at <http://www.webcitation.org/67UIABY8M>
- United States Census Bureau. [accessed January 2012] 2000 SF3 Sample Data. 2012b. <http://factfinder2.census.gov/faces/nav/jsf/pages/searchresults.xhtml?ref=top&refresh=t>. Archived by WebCite at <http://www.webcitation.org/67UIC8M7V>
- United States Census Bureau. [accessed January 2012] ACS Demographic and Housing Estimates: 2005–2009. 2012c. [http://factfinder2.census.gov/faces/tableservices/jsf/pages/productview.xhtml?pid=ACS\\_09\\_5YR\\_DP5YR5&prodType=table](http://factfinder2.census.gov/faces/tableservices/jsf/pages/productview.xhtml?pid=ACS_09_5YR_DP5YR5&prodType=table). Archived by WebCite at <http://www.webcitation.org/67UI8EsZx>
- Warner, M.; Chen, LH.; Makuc, DM. NCHS Data Brief. Hyattsville: National Center for Health Statistics; 2009. Increase in Fatal Poisonings Involving Opioid Analgesics in the United States, 1999–2006.

- Wunsch M, Nakamoto K, Behonick G, Massello W. Opioid deaths in rural Virginia: a description of the high prevalence of accidental fatalities involving prescribed medications. *Am. J. Addict.* 2009; 18:5–14. [PubMed: 19219660]
- Zacny J, Bigelow G, Compton P, Foley K, Iguchi M, Sannerud C. College on Problems of Drug Dependence taskforce on prescription opioid non-medical use and abuse: position statement. *Drug Alcohol Depend.* 2003; 69:215–232. [PubMed: 12633908]

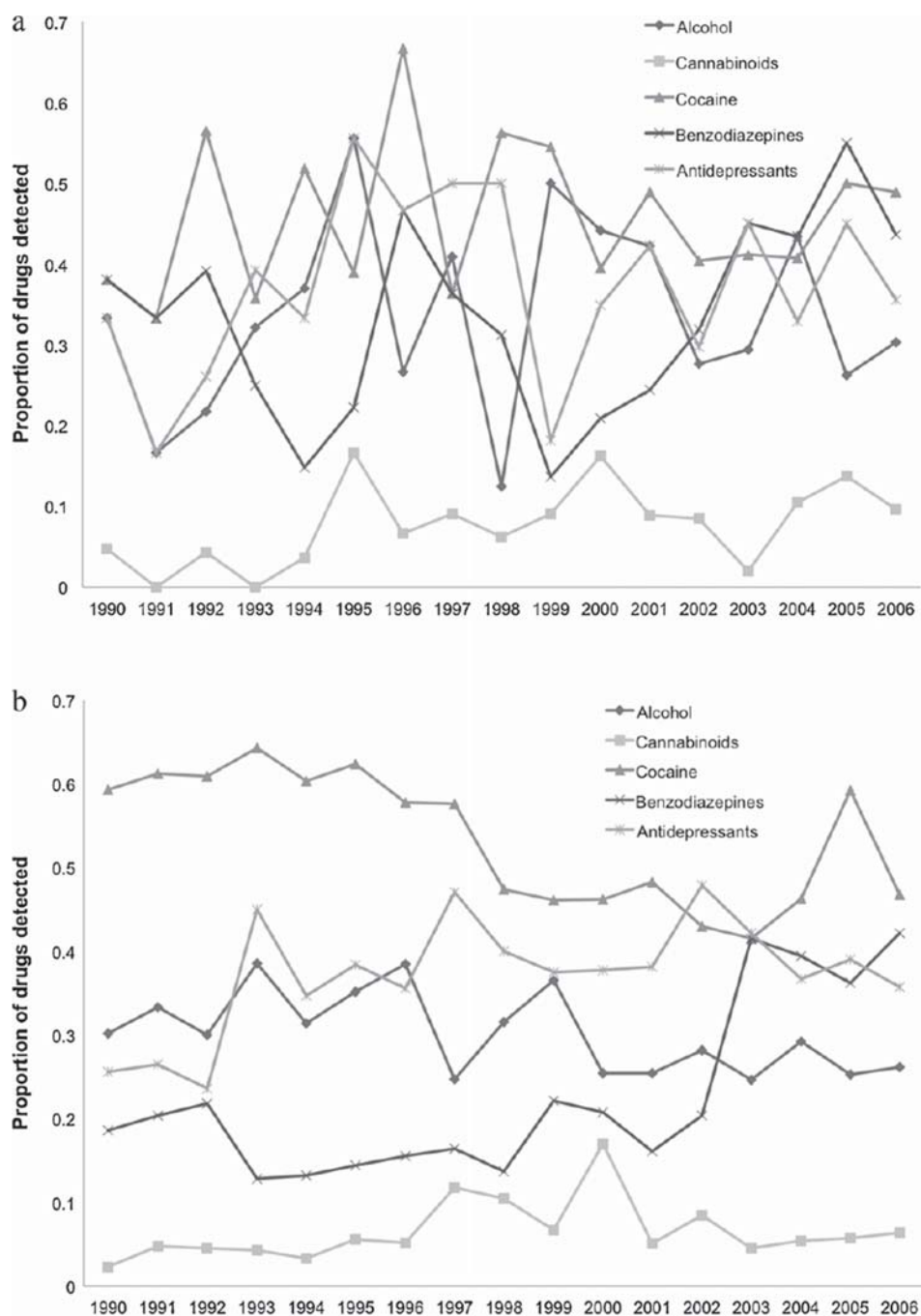


**Fig. 1.**

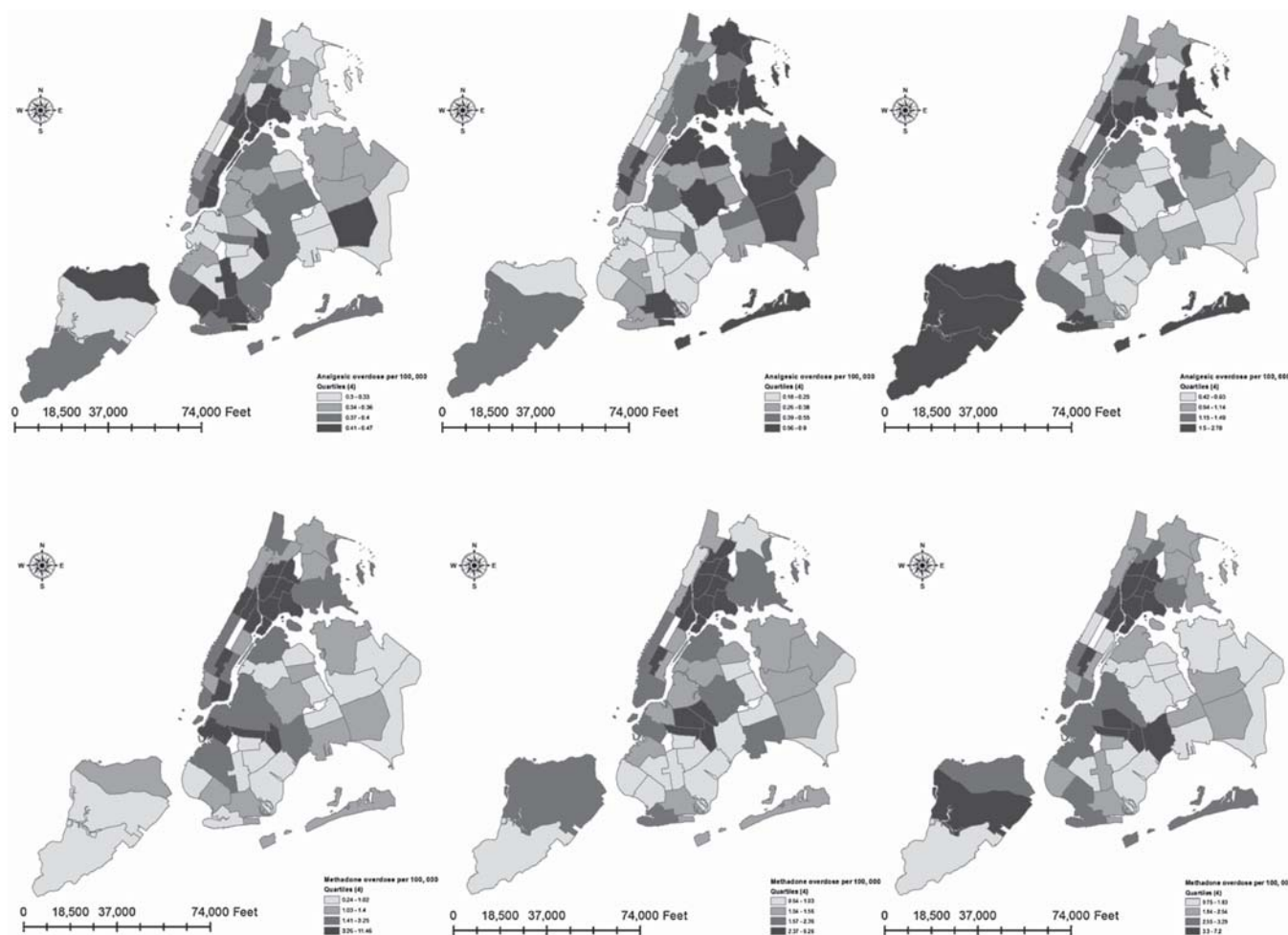
Standardized overdose death rates by type of drug, New York City, 1990–2006.



**Fig. 2.**  
 (a) Analgesic-induced death rates by race/ethnicity and sex, New York City, 1990–2006. (b)  
 Methadone-induced death rates by race/ethnicity and sex, New York City, 1990–2006.

**Fig. 3.**

(a) Proportion of analgesic-induced overdose deaths with other drugs detected, by type of drug. (b) Proportion of methadone-induced overdose deaths with other drugs detected, by type of drug.



**Fig. 4.** Age-adjusted analgesic- and methadone-induced overdose death rates by community district, New York City. Maps are presented in three panels (from left to right) for the periods of 1990–1995, 1996–2000, and 2001–2006. Analgesic overdose fatalities are presented in the upper row, and methadone overdose fatalities are presented in the lower row.

**Table 1**Characteristics of analgesic- and methadone-induced overdose deaths, New York City, 1990–2006.<sup>a,b</sup>

	<u>Analgesic overdose</u>		<u>Methadone overdose</u>	
	<i>N</i>	%	<i>N</i>	%
Total	681	100	2207	100
Sex				
Male	488	71.66	1522	68.96
Female	193	28.34	685	31.04
Race/ethnicity				
White	409	60.06	808	36.61
Black	116	17.03	679	30.77
Hispanic	148	21.73	704	31.90
Age				
15–24	45	6.61	67	3.04
25–34	134	19.68	347	15.72
35–44	268	39.35	962	43.59
45–54	190	27.90	684	30.99
55–64	44	6.46	146	6.62
Place of injury				
Residence	532	82.74	1632	79.92
Workplace	3	0.47	9	0.44
Jail/prison	1	0.16	13	0.64
Hospital/doctor's office/nursing home	10	1.56	52	2.55
Public transportation or car	18	2.80	57	2.79
Hotel (in room or elsewhere)	38	5.91	88	4.31
Bar/restaurant	4	0.62	5	0.24
Streets/lot/school yard	24	3.73	137	6.71
Parks or water	5	0.78	19	0.93
Building (public, abandoned or unspecified)	8	1.24	30	1.47
Unknown	38	5.60	165	7.50
Borough of death				
Manhattan	167	24.52	611	27.68
Bronx	140	20.56	551	24.97
Brooklyn	151	22.17	618	28.00
Queens	171	25.11	336	15.22
Staten Island	52	7.64	91	4.12
Heroin as a contributing cause				
No	377	55.36	1646	60.07
Yes	304	44.64	1094	39.93
Drugs detected				
Alcohol detected				
No	437	64.17	1492	67.60

	<u>Analgesic overdose</u>		<u>Methadone overdose</u>	
	<i>N</i>	%	<i>N</i>	%
Yes	230	33.77	664	30.09
Cannabinoids detected				
No	408	59.91	1148	52.02
Yes	60	8.81	140	6.34
Cocaine detected				
No	370	54.33	1034	46.85
Yes	311	45.67	1173	53.15
Benzodiazepines detected				
No	428	62.85	1667	75.53
Yes	253	37.15	540	24.47
Antidepressants detected				
No	426	62.56	1384	62.71
Yes	255	37.44	823	37.29

<sup>a</sup>The two groups are not exclusive – there are overlapping cases of analgesic- and methadone-induced overdose fatalities.

<sup>b</sup>Some frequencies do not add up to 100% due to missing data.



Associations with analgesic- or methadone-induced overdose deaths relative to heroin-induced overdose deaths, New York City, 1990–2006.<sup>a,b</sup>

Table 2

	Analgesic-induced overdose deaths			Methadone-induced overdose deaths		
	Unadjusted		Adjusted	Unadjusted		Adjusted
	OR	95% CI	OR	95% CI	OR	95% CI
Sex						
Female	1.88	(1.49, 2.38)	1.57	(1.21, 2.04)	2.58	(2.26, 2.93)
Race/ethnicity						
White						
Black	0.43	(0.32, 0.58)	0.74	(0.54, 1.02)	1.33	(1.16, 1.53)
Hispanic	0.32	(0.24, 0.43)	0.50	(0.37, 0.69)	0.97	(0.84, 1.12)
Age						
15–24	1.17	(0.77, 1.78)			0.39	(0.28, 0.55)
25–34	0.96	(0.72, 1.29)			0.56	(0.47, 0.66)
35–44						
45–54	0.95	(0.73, 1.25)			1.24	(1.07, 1.43)
55–64	1.25	(0.82, 1.90)			1.36	(1.05, 1.76)
Place of injury						
Residence						
Other inside	0.50	(0.36, 0.71)	0.54	(0.38, 0.78)	0.72	(0.60, 0.86)
Outside	0.38	(0.22, 0.67)	0.54	(0.29, 0.96)	0.78	(0.63, 0.98)
Borough of death						
Manhattan						
Bronx	0.49	(0.34, 0.71)	0.55	(0.37, 0.81)	0.99	(0.84, 1.17)
Brooklyn	0.84	(0.62, 1.12)	0.79	(0.58, 1.08)	1.19	(1.02, 1.38)
Queens	1.80	(1.35, 2.41)	1.42	(1.03, 1.94)	1.08	(0.90, 1.30)
Staten Island	2.58	(1.68, 3.96)	1.51	(0.93, 2.44)	1.70	(1.26, 2.31)
Drugs detected						
Alcohol detected	0.61	(0.49, 0.77)	0.65	(0.50, 0.83)	0.47	(0.42, 0.54)
Cannabis detected	1.21	(0.84, 1.73)			0.70	(0.56, 0.89)
Cocaine detected	0.66	(0.54, 0.82)	0.75	(0.60, 0.95)	0.82	(0.73, 0.93)

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	Analgesic-induced overdose deaths			Methadone-induced overdose deaths		
	Unadjusted	OR	95% CI	Unadjusted	OR	95% CI
Benzodiazepines detected	3.79		(3.04, 4.74)	2.81		(2.20,3.58)
Antidepressants detected	2.27		(1.82, 2.84)	1.83		(1.43, 2.33)
				3.51		(3.09, 3.98)
				2.98		(2.60, 3.42)

<sup>a</sup> Separate logistic regression models were estimated to contrast analgesic- vs. heroin-induced overdose deaths, and methadone- vs. heroin-induced overdose deaths.

<sup>b</sup> Overlapping cases of analgesic- and heroin-induced overdose deaths were removed for the analgesic-vs. heroin-induced overdose contrast, while overlapping cases of methadone- and heroin-induced overdose deaths were removed for the methadone- vs. heroin-induced overdose contrast.